

REMARKS/ARGUMENTS

Upon entry of the instant amendments, claims 1-22 and 32 are pending. Claims 23-31 and 33 were withdrawn. Claims 1, 3, and 14-18 have been amended without any intention of disclaiming equivalents thereof. No new matter is added.

Rejoinder of Groups I and II

Applicants acknowledge the rejoinder of group I (claims 1-17 and 32) and group II (claims 18-22).

Rejection Under 35 U.S.C. § 112

The Examiner rejected claims 14-17 under 35 U.S.C. § 112, second paragraph. Applicants submit that the claims have been amended to provide correct antecedent basis and respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 102(b) over Kenji et al.

The Examiner rejected claims 1-3, 6-7, 10-13, 18, and 21-22 under 35 U.S.C. § 102(b), contending that they are anticipated by Kenji et al. (EP 0 476 545). Applicants traverse the rejection to the extent it is maintained over the claims as amended.

Anticipation under 35 U.S.C. § 102 requires that all of the elements and limitations of the claims at issue be found within a single prior art reference. *Carella v. Starlight Archery and Pro Line Co.*, 804 F.2d 135, 231 U.S.P.Q. 644 (Fed. Cir. 1986).

Kenji et al. does not teach all the elements and limitations of Applicants' claims as amended. Kenji et al. disclose immunoassays for detecting a target substance, using an antibody that reacts with the target substance, wherein the antibody is also bound to a fluorescent substance, and a second antibody bound to a quencher, the second antibody capable of binding a different epitope of the target molecule. The only detection method described in Kenji et al. is the detection of fluorescence and the quenching of fluorescence. Kenji et al. does not disclose determining turbidity or agglutination and therefore does not disclose Applicants' claimed

invention. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claims 1-3, 6-7, and 10-13.

Regarding claims 18 and 21-22, Applicants submit that Kenji et al. does not disclose a composition comprising protein S and C4BP and therefore does not disclose Applicants' claimed invention. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claims 18 and 21-22.

Rejections Under 35 U.S.C. § 103(a) over Kenji et al. in view of Koike et al.

The Examiner rejected claims 5-6, 8-9, 19-20, and 32 under 35 U.S.C. § 103(a), contending that they are unpatentable over Kenji et al. (EP 0 476 545) in view of Koike et al. (US Patent No. 5,187,067). Applicants traverse the rejection to the extent it is maintained over the claims as amended.

The proper standard for evaluating obviousness requires a determination of (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have a reasonable expectation of success. *See In re Vaeck*, 947 F.2d 488, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Both the suggestion and the reasonable expectation of success must be found in the prior art, not in Applicant's disclosure. *See id.* citing *In re Dow Chemical Co.* 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988). Finally, section 103 requires that the suggestion or incentive to combine prior art references must be derived from the teachings of the references. *See ACS Hosp. Systems, Inc. v. Montefiore Hosp.* 732 F.2d 1572, 1577, 21 U.S.P.Q. 929, 933 (Fed. Cir. 1984).

Applicants submit that there is no motivation in either Kenji et al. or Koike et al. to combine their disclosures to make Applicants' claimed invention and even if, *arguendo*, such motivation were found and the disclosures of the references were combined, such a combination would not teach Applicants' invention. Kenji et al. does not disclose turbidity or agglutination

assays. Koike et al. does not correct the deficiency of Kenji et al. Koike et al. discloses a method for determining free protein S in a sample using a primary antibody fixed to an insoluble solid carrier and a labelled second antibody that binds to a second epitope on protein S. Koike et al. disclose using the assay means enzyme immunoassay (EIA) and radioimmunoassay (RIA) (column 13, lines 4-7). Koike et al. does not disclose or suggest turbidity or agglutination assays. Koike et al. also does not provide an expectation of success that measurable turbidity or agglutination would take place between a first particle bound to a second member and a second particle bound to a third member, when the second and third members are bound to the first member. Applicants also submit that the rejection of claim 9 under §103 is improper, because Koike et al. does not disclose a second member that is C4BP. Thus, even if the references were combinable, they would not teach Applicants' claimed methods. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claims 5-6 and 8-9.

In addition, Koike et al. does not disclose a composition for detecting an unbound form of a first member of a binding pair, the binding pair comprising a first and a second member that bind to each other, wherein a first particle is bound to the second member and a second particle is bound to a third member, wherein the second and third member bind to the first member at different epitopes, wherein the first member comprises protein S and the second member comprises C4BP. This is because Koike et al. is directed only to the use of antibodies to either free protein S or the C4BP-protein S complex, not the use of C4BP itself as one of the binding partners (i.e., members) in the assay for detecting free protein S. In particular, Applicants submit that the rejection of claim 20 under § 103 is improper, because Koike et al. does not disclose a second member that is not an antibody. Thus, even if the references were combinable, they would not teach Applicants' claimed compositions. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claims 19-20 and 32.

Rejections Under 35 U.S.C. § 103(a) over Kenji et al. in view of Noguchi et al.

The Examiner rejected claim 4 under 35 U.S.C. § 103(a), contending that it is unpatentable over Kenji et al. (EP 0 476 545) in view of Noguchi et al. (US Patent No. 4,843,021). Applicants traverse the rejection to the extent it is maintained over the claims as amended.

Applicants submit that there is no motivation in either Kenji et al. or Noguchi et al. to combine their disclosures to make Applicants' claimed invention and even if, *arguendo*, such motivation were found and the disclosures of the references were combined, a skilled artisan would have no expectation of success that the methods of Noguchi et al. combined with the methods of Kenji et al. would produce Applicants' invention.

Noguchi et al. does not correct the deficiency of Kenji et al. Noguchi et al. discloses the use of a calibration curve for determining the concentration of a substance in a sample assayed using immunological methods. Noguchi et al. does not disclose detecting turbidity or agglutination generated by the binding of two members to an antigen at different epitopes, wherein each member is complexed to a particle, but rather Noguchi et al. describes the low level of turbidity that is generated when an antigen binds to an antibody. The methods disclosed in Noguchi et al. use only one antibody (i.e., "monotest reagent") per reaction to detect a component of a sample and not two members (e.g., antibodies or C4BP) as required by Applicants' claims. There would be no expectation of success that the calibration curves and turbidity analysis of Noguchi et al. would work when the components include a third member (e.g., antibody) that is also bound to a particle, which also is not described in Noguchi et al. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claim 4.

Rejections Under 35 U.S.C. § 103(a) over Kenji et al. in view of Mischak et al.

The Examiner also rejected claims 14-17 under 35 U.S.C. § 103(a), contending that they are unpatentable over Kenji et al. (EP 0 476 545) in view of Mischak et al. (US Patent No.


6,124,430). Applicants traverse the rejection to the extent it is maintain over the claims as amended.

Applicants submit that there is no motivation in either Kenji et al. or Mischak et al. to combine the references to make Applicants' claimed invention and even if, *arguendo*, such motivation were found and the disclosures of the references were combined, such a combination would not teach Applicants' invention. Kenji et al. does not disclose turbidity or agglutination assays. Mischak et al. does not correct the deficiency of Kenji et al. because it also does not disclose turbidity or agglutination assays. Mischak et al. discloses typical sandwich assays and competition assays using two antibodies wherein one of the antibodies captures the antigen in a sample (e.g., onto a microtiter plate) and the other antibody is labeled with a detectable label and binds to another epitope on the antigen. Mischak et al. discloses only detecting the label, not detecting any other physical characteristic of the antigen-antibody reaction, such as agglutination or turbidity. Mischak et al. also does not disclose a third member (e.g., antibody) that is bound to a particle such that the reaction between a second member-first particle complex and a third member-second particle complex agglutinate when they bind to a first member (e.g., antigen). There would be no expectation of success that the sandwich and competition assays of Mischak et al. would work in an agglutination assay format when the components include a third member (e.g., antibody) that is also bound to a particle. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claims 14-17.

CONCLUSION

In view of the following amendments and remarks, Applicants respectfully request that the outstanding rejections be reconsidered and withdrawn. Applicants respectfully urge that all claims are in condition for allowance and request prompt and favorable action on the instant application.

Respectfully submitted,



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Date: August 2, 2004
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